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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/621,593	07/21/2000	Nanda de Groot	4497US	4769

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/621,593	DE GROOT ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/17/03*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-36 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *26-34 and 36* is/are allowed.

6)☒ Claim(s) *35 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Final Rejection

Claims 26-36 and 38 are pending examination.

Applicants' traversal, the amendment to claims 26-36; the cancellation of claim 37, and the addition of claim 38 in paper filed on 11/17/03 is acknowledged and considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 35 remains and claim 38 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using interferon-γ, Il-1, Il-4, TNF-alpha to enhance expression of an endogenous pIgR in a transgenic non-human mammalian animal, whose genome comprises a DNA construct comprising a nucleic acid encoding the pIgR protein operably linked to the endogenous promoter for pIgR, does not reasonably provide enablement for using any protein, including an antigen or interferon-γ, Il-1, Il-4, TNF-alpha with any promoter (endogenous or exogenous) operatively linked to the nucleic acid encoding pIgR protein to enhance expression of pIgR in said non-human mammalian animal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of

experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention is directed to the making and using a transgenic mammalian farm animal whose genome comprises a stably integrated recombinant nucleic acid encoding a polymeric immunoglobulin receptor (pIgR) protein, wherein said animal over-expresses said pIgR protein compared to the expression of the pIgR protein in a wild-type animal. The invention lies in the field of producing transgenic non-human animals.

The art of record teaches how to make and use transgenic mammals whose genome expresses a heterologous gene product (US Patent No. 5,895,833).

The specification displays transgenic mice whose genome comprises a recombinant nucleic acid encoding a murine pIgR capable of transporting an immunoglobulin from a mammary epithelial cell's basolateral side to the cell's apical side (pages 2 and 3). The specification further provides teachings that pIgR is capable of transporting dimeric IgA across the epithelial cells of mucosal surfaces into the external secretions and raising the concentration of IgA relative to IgG in external secretion (pages 6 and 7).

The specification provides sufficient guidance and/or factual evidence for one skilled in the art to make and use a transgenic non-human mammalian animal whose genome comprises a recombinant nucleic acid encoding a polymeric immunoglobulin receptor (pIgR) protein operatively linked to a promoter, wherein said protein is over-expressed in the mammary gland of said animal.

However, with respect to new claim 38, which embraces using an antigen or interferon-γ, Il-1, Il-4, TNF-alpha to enhance endogenous expression of pIgR expression in said transgenic non-human mammalian animal; and amended claim 35, which embraces administering any

protein to said transgenic non-human mammalian animal to enhance endogenous expression of pIgR expression in said non-human mammalian animal, the claims are not considered fully enabled. The specification cites art that teaches that *in vitro* pIgR expression is enhanced when a protein selected from the group consisting of interferon-γ, interleukin-1, interleukin-4, and tumor necrosis factor-α. The specification and the art of record do not define what type of promoter was used for enhanced *in vitro* expression of pIgR. One skilled in the art, without evidence to the contrary, would conclude that the endogenous promoter for pIgR was used in the *in vitro* assay. Claim 35 embraces using any protein, including an antigen or interferon-γ, Il-1, Il-4, TNF-alpha set forth in claim 38 with any promoter (endogenous or exogenous) operatively linked to the nucleic acid encoding pIgR protein to enhance expression of pIgR in a transgenic mammalian farm animal. However, the specification fails to provide sufficient guidance for one skilled in the art to use a promoter (e.g. casein promoter, LTR promoter, etc.) to enhance pIgR expression other than the endogenous promoter for pIgR without an undue amount of experimentation. The as-filed specification does not teach what nucleotides sequences of the endogenous promoter are considered essential for enhancing the over-expression of pIgR in the presence of the claimed proteins. In addition, the specification does not teach what promoters are able to enhance pIgR expression in the presence of the claimed proteins. The art of record does not teach what types of promoters can enhance the expression of pIgR in the presence of the claimed proteins. With respect to the specification contemplating that any protein can be administered to said transgenic mammalian animal to enhance expression of endogenous pIgR in said animal.

The court in Enzo 188 F.3d at 1374, 52 USPQ2d at 1138 states:

It is well settled that patent applications are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed.
In re Vaeck, 947 F.2d 48, 496 & n.23. 30 USPQ2d 1438, 1445 &n23 (Fed. Cir. 1991)(citation omitted). Here, however, the teachings set forth in the specification provide no more than a "plan" or "invitation" for those of skill in the art to experiment...; they do not provide sufficient guidance or specificity as to how to execute that plan. See Fiers v. Revel. 984 F.2d.1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); In re Wright, 999 F.2d...[1557], 1562, 27 USPQ2d...[1510], 1514. [Footnote omitted].

On this record, it is that the specification provides no more than a plan or invitation for experimentation in view of the absence in the art of record and the as-filed specification to use any protein, for those skilled in the art to experiment with any protein and promoter combination, so as to provide an enhanced method of expressing pIgR as intended by the as-filed specification at the time the invention was made.

See also Genetech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997)

> ("Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the public to understand and carry out the invention.")

In view of the art of record and the lack of guidance provided by the specification; the specification does not provide reasonable detail for what proteins are required for different proteins contemplated for use in the claimed method, and it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from the prior art cited in the specification in the specification to using the claimed invention. Thus, in view of the In Re Wands Factors, the claims are not considered fully enabled.

In conclusion, the as-filed specification and claims coupled with the art of record at the time the invention was made only enable one skilled in the art to use an interferon-γ, Il-1, Il-4, TNF-alpha to enhance expression of an endogenous pIgR in a transgenic non-human mammalian animal, whose genome comprises a DNA construct comprising a nucleic acid encoding the pIgR protein operably linked to the endogenous promoter for pIgR. Given the lack of sufficient guidance or direction provided by the specification for using any protein to enhance endogenous expression of pIgR in the claimed transgenic non-human mammalian animal and the lack of evidence in the art of record for using any protein and promoter combination to practice the claimed invention, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicants' disclosure.

Applicant's arguments filed 11/17/03 have been fully considered but they are not persuasive because the applicants' did not address the rejection for claim 35 set forth under 112 first paragraph.

Response to Arguments

Applicant's arguments, filed 11/17/03, with respect to objection have been fully considered and are persuasive. The objection of claim 26 has been withdrawn.

Applicant's arguments, filed 11/17/03, with respect to 112 first paragraph rejection have been fully considered and are persuasive. The rejection of claims 26-34 and 36 has been withdrawn because of the amendment to the claims.

Applicant's arguments, filed 11/17/03, with respect to 112 second paragraph rejection have been fully considered and are persuasive. The rejection of claims 26-37 has been withdrawn because of the amendment to the claims and the cancellation of claim 37.

Conclusion

Claims 26-34 and 36 are in condition for allowance because the claims are free of the prior art of record.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764.

The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER